EXHIBIT B-1

Expert Report of
John (Jeb) Hallett, M.D.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF SOUTH CAROLINA
CHARLESTON DIVISION

PALMETTO PHARMACEUTICALS LLC Plaintiff, v. ASTRAZENECA PHARMACEUTICALS LP Defendant.	C/A No. 2:11-CV-00807- SB-JDA **EXPERT REPORT OF JOHN (JEB) HALLETT, MD**

INTRODUCTION

1. This report is being submitted in the matter of Palmetto Pharmaceuticals LLC v. AstraZeneca Pharmaceuticals LP No. 2:11-CV-00807- SB-JDA in the United States District Court for South Carolina Charleston Division.

BACKGROUND AND EXPERIENCE

2. I am a vascular surgeon and the medical director of the Roper St. Francis Heart and Vascular Center in Charleston, South Carolina ("Roper St. Francis"). I am board certified in vascular surgery and am listed in Best Doctors in America for my expertise in abdominal aortic aneurysms, carotid artery disease, and peripheral vascular disease, including renal vascular hypertension.

3. I earned a Bachelor of Science degree from the United States Air Force Academy in 1969 and my Doctor of Medicine degree from Duke University in 1973. I was a medical

resident from 1973 until 1978 and a staff surgeon from 1978 to 1979 at Wilford Hall, United States Air Force Medical Center, Lackland Air Force Base, Texas.

4. In 1979, I relocated to Massachusetts General Hospital, Harvard Medical School where I was a Clinical and Research Fellow in Vascular Surgery.

5. After completing vascular surgery training at Harvard Medical School, Massachusetts General Hospital, I went back to Wilford Hall, United States Air Force Medical Center and served as Chief of Vascular Surgery. I held this position from 1980 until 1984. In 1984, I became a Staff Vascular Surgeon at the Mayo Clinic in Rochester Minnesota. I remained at this position until 2001. While at the Mayo Clinic, I was the Vascular Surgery Fellowship Program Director 1990 to 1997, Director of Education in the Department of Surgery from 1990 to 2001, Director of Mayo Gonda Vascular Center 1997-2001, and Associate Dean for Faculty Affairs at the Mayo Medical School 1998-2001.

6. In 2001, I was recruited to Eastern Maine Health Care to establish the Vascular Care Center of Maine. I was Director, Vascular Care of Maine, Eastern Maine Medical Center from 2001 to 2004. In 2004, I moved to my current position at Roper St. Francis Heart and Vascular Center in Charleston, South Carolina.

7. In addition to my clinical practice, I am co-author of the textbook Comprehensive Vascular and Endovascular Surgery and the original author of the Handbook of Patient Care in Vascular Diseases. I have authored or co-authored more than 100 peer-reviewed publications and have given numerous lectures in the field of cardiovascular medicine and vascular surgery.

8. I am a past member of the editorial board for the Annals of Vascular Surgery (1989-1997) and the Journal of Vascular Surgery (1994-2001). I am a current member of the editorial board for International Angiology, Merck Manual, and The Vascular Specialist.

9. In my career, I have received a number of awards, including the The Oliver H. Beahrs Distinguished Surgical Lecture; Uniformed Services University of the Health Sciences, 2008; Roper St Francis Foundation Physician Champion Award for Outstanding Leadership, 2006; Linton Lecture in Vascular Surgery, Harvard Medical School, 2003. I have also been honored from my teaching. These awards include multiple Teacher of the Year Awards and induction into the Mayo Medical School Teaching Hall of Fame.

10. My current research involves ischemic events related to bone marrow transplants and my current grant for this research runs through 2014.

11. My attached Curriculum Vitae (Ex. A) provides the specifics of my relevant experience.

COMPENSATION

12. I am being compensated for my expert work at a rate of $500.00 per hour.

MATERIALS REVIEWED

13. A detailed list of the materials I have reviewed in preparation of this report is attached as Ex. B.

PRIOR TESTIMONY

14. I have not testified in court in the past four years. I have been deposed in the past four years.

OPINION

Cardiovascular Disease Screening at Roper St. Francis

15. At Roper St. Francis we have an innovative program to screen patients for risks factors associated with cardiovascular disease. We use ultrasound for vascular screening the carotid arteries, screening for abdominal aortic aneurysm, and ankle-brachial index measurements with blood pressure cuffs and Doppler. We also perform cardiac calcium scoring using CT scanning. The Roper St. Francis program is inexpensive for the patient and provides an accurate assessment of cardiovascular risk. The results from this screening are used by our physicians to decide whether to prescribe a statin, like Crestor®, to our patients.

16. It has long been known that plaque formation and instability are leading causes of acute coronary events. For example, a dislodged plaque can form an occlusion, and thereby lead to a heart attack or stroke. Statins have been viewed as providing beneficial effects on patients by increasing nitric oxide (NO) production, reducing inflammation, stabilizing plaques and improving endothelial function. S.I. McFarlane et al., *Pleiotropic Effects of Statins: Lipid Reduction and Beyond,* 87 J. Clin. Endocrinol. Metab. 1451-58, 1451 (2002) (Ex. C).

17. Statins have been shown to have a broad spectrum of cholesterol-independent protective effects, including plaque stabilization and preservation of endothelial function. C. P. Tiefenbacher et al., *Reduction of Myocardial Infarct Size by Fluvastatin,* 285 Am.J. Physiol. Heart Circ. Physiol. H59-H64, H59 (2003) (Ex. D.)

18. It has long been known that increased C reactive protein (CRP) levels are implicated in the development of complex angiographic stenoses, which are high risk coronary plaques. Ramón Arroyo-Espliguero et al., *C-reactive protein elevation and disease activity in patients with coronary artery disease,* 25 European Heart J. 401-408, 402 (2004) (Ex. E). Indeed, the authors conclude:

> CRP levels predict future cardiovascular events independently of CAD severity and correlate with number of angiographically complex coronary artery stenosis in patients with ACS. Thus, CRP levels are a marker of atheromatous plaque vulnerability and CAD activity.

See Abstract at 401.

19. In 2005, Atushi Tanaka et al. reported that ruptured plaques are associated with elevated CRP levels. *Multiple Plaque Rupture and C-Reactive Protein in Acute Myocardial Infarction,* 45 J. Amer. Coll. Cardiol. 1594-99, 1597 (2005) (Ex. F).

20. Rubin et al. used CT scans to evaluate the relationship between high CRP levels and plaque formation. The authors concluded that:

> [i]n an asymptomatic population, increasing levels of CRP are associated with the prevalence of any plaque and MCAP [Mixed-Calcified Plaque], the extent of MCAP, and the presence of significant coronary stenosis. Our study results suggest that the increased cardiovascular risk associated with increased levels of CRP could be due in part to a higher prevalence of MCAP, which has been shown to possess some of the key elements observed in unstable plaques.

Rubin et al., *Association Between High-Sensitivity C-Reactive Protein and Coronary Plaque Subtypes Assessed by 64-Slice Coronary Computed Tomography Angiography in an Asymptomatic Population*, 4 Circ. Cardiovasc. Imaging, 201-09, 207-08 (2011) (Ex. G).

21. As explained at page 203 of the Rubin publication, the asymptomatic patients having higher CRP levels examined in the Rubin CT study had LDL-C levels of 123 ± 34 mg/dL, which means that a set of the patients met the less than 130 mg/dL LDL-C level set forth in Indications 1.6 and 14.8 of the Crestor® package insert (Ex. H).

22. Below are Indications 1.6 and 14.8 of the Crestor® package insert:

1.6 Primary Prevention of Cardiovascular Disease

In individuals without clinically evident coronary heart disease but with an increased risk of cardiovascular disease based on age ≥50 years old in men and ≥60 years old in women, hsCRP ≥2 mg/L, and the presence of at least one additional cardiovascular disease risk factor such as hypertension, low HDL-C, smoking, or a family history of premature coronary heart disease, CRESTOR is indicated to:

- reduce the risk of stroke
- reduce the risk of myocardial infarction
- reduce the risk of arterial revascularization procedures

Package insert at 1.6.

14.8 Primary Prevention of Cardiovascular Disease

In the Justification for the Use of Statins in Primary Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER) study, the effect of CRESTOR (rosuvastatin calcium) on the occurrence of major cardiovascular (CV) disease events was assessed in 17,802 men (≥50 years) and women (≥60 years) who had no clinically evident cardiovascular disease, LDL-C levels <130 mg/dL (3.3 mmol/l) and hs-CRP levels ≥2 mg/L. The study population had an estimated baseline coronary heart disease risk of 11.6% over 10 years based on the Framingham risk criteria and included a high percentage of patients with additional risk factors such as hypertension (58%), low HDL-C levels (23%), cigarette smoking (16%), or a family history of premature CHD (12%). Study participants had a median baseline LDL-C of 108 mg/dL and hsCRP of 4.3 mg/L. Study participants were randomly assigned to placebo (n=8901) or rosuvastatin 20 mg once daily (n=8901) and were followed for a mean duration of 2 years. The JUPITER study was stopped early by the Data Safety Monitoring Board due to meeting predefined stopping rules for efficacy in rosuvastatin-treated subjects.

Package insert at 14.8.

23. The papers discussed above show that the patients we are screening for plaque status will have elevated levels of CRP. Based upon the known relationship between elevated CRP levels and reduced nitric oxide production (discussed below), these patients showing plaques will benefit by administration of a statin to increase nitric oxide production.

CRP, NO and Cardiovascular Disorders

24. Cardiovascular professionals read the scientific literature to keep up with medical advances and the latest knowledge in the field. The community of cardiovascular professionals have known about and understood the importance of the biological relationship between elevated CRP and decreased NO production for about a decade if not longer. Dr. Verma's laboratory was one of the first to show the effect that CRP has on NO production. In the 2002 publication, *A Self-Fulfilling Prophecy: C-Reactive Protein Attenuates Nitric Oxide Production and Inhibits Angiogenesis*, 106 Circulation 913-919 (2002) (Ex. I), this group found that elevated levels of CRP decreases production of NO.

> CRP, at concentrations known to predict adverse vascular events, directly quenches the production of the NO . . . .

Id. at 913.

25. The importance of the relationship between elevated CRP and decreased NO production was such that Dr. Paul M. Ridker, AstraZeneca's lead investigator for the JUPITER trial, in his publication describing the rationale for JUPITER cites Dr. Verma's study:

> evidence has recently accumulated that shows CRP to be a direct participant in the atherothrombotic process capable of augmenting the innate inflammatory response, triggering expression of adhesion molecules and monocyte chemoattractant protein-1, attenuating expression of endothelial NO synthase….

Ridker, *Rosuvastatin in the Primary Prevention of Cardiovascular Disease Among Patients With Low Levels of Low-Density Lipoprotein Cholesterol and Elevated High-Sensitivity C-Reaction Protein: Rationale and Design of the JUPITER Trial*, 108 Circulation 2292-2297, 2292 (2003) (Ex. J).

26. JUPITER stands for **J**ustification for the **U**se of statins in **P**revention: an **I**ntervention **T**rial **E**valuating **R**osuvastatin. The JUPITER trial was designed to test whether patients without hyperlipidemia who had elevated CRP levels and other risk factors would benefit from Crestor® administration. The JUPITER trial was funded by AstraZeneca and led to indications 1.6 and 14.8 reproduced above.

27. It is important to note that Dr. Verma's observation was not a one-time event. His results and conclusions have been confirmed a number of times from the 2002 study to the present day.

28. For example, in 2003, Dr. Verma and co-authors reported again that CRP quenches NO production:

> CRP, at concentrations known to predict diverse vascular insults, profoundly quenches nitric oxide (NO) synthesis, while augmenting the release of endothelin-1 (ET-1) and upregulating adhesion molecules and chemoattractant chemokines, uncovering a proinflammatory and proatherosclerotic phenotype.

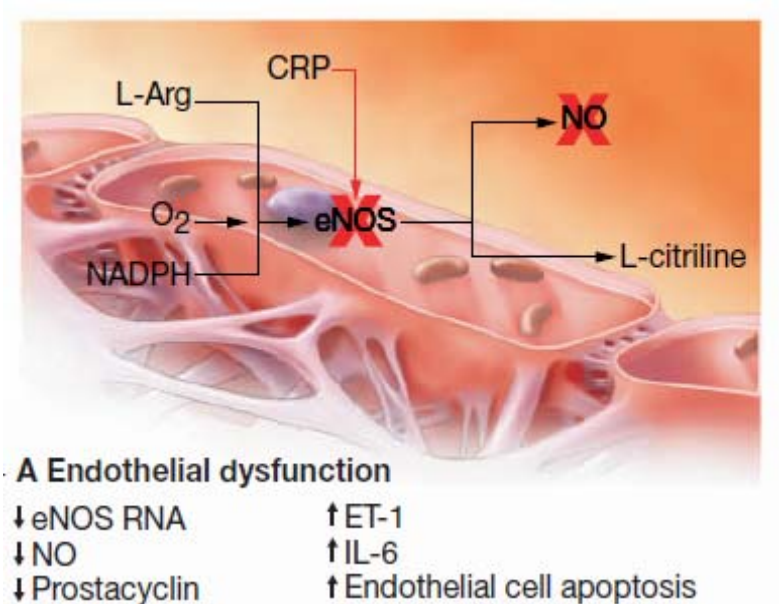
Chao-Hung Wang et al. , *C-Reactive Protein Upregulates Angiotensin Type 1 Receptors in Vascular Smooth Muscle*, 107 Circulation 1783-1790, 1783 (2003) (Ex. K).

29. In 2005, Dr. Verma again reported on this topic, and this time was joined as an author by Dr. Ridker. This team reported on the current knowledge in the field of CRP research in their review article, Subodh Verma et al., *C-reactive protein comes of age*, 2 Nature Clinical Practice Cardiovascular Medicine, 29-36 (2005) (Ex. L). In this publication Drs. Verma and Ridker stated:

> Endothelial dysfunction, which implies the diminished production or availability of nitric oxide (NO), an increase in endothelium-derived contracting factors, such as endothelin-1, angiotensin or both, sets the stage for inflammation and atherogenesis. CRP appears to serve not only as a marker of this pathologic inflammatory process but also as an active partaker in all stages of atherogenesis, since it is present in atherosclerotic lesions but not in the normal vessel wall.
>
> Laboratory data from our group and others suggests that human recombinant CRP, at concentrations known to predict vascular disease, elicits a multitude of effects on endothelial biology favoring a proinflammatory and proatherosclerotic phenotype. CRP potently downregulates endothelial NO synthase transcription and destabilizes endothelial NO synthase mRNA *in vitro*, resulting in decreased basal and lowered release of stimulated NO, a key endothelium-derived relaxing factor.

Id. at 31 and 33

30. In Figure 2, Drs. Verma and Ridker show the CRP/NO relationship diagrammatically. Figure 2 illustrates CRP inhibition of eNOS which in turn leads to a decrease in NO production.



Id. at 32, Figure 2 (in part).

31. More recently, Dr. Schneider's group reported that patients showed improved vascular function after seven weeks of treatment with Crestor®. C. Ott et al., *Rosuvastatin Improves Pulse Wave Reflection by Restoring Endothelial Function*, Microvascular Research 2012, online at http://dx.doi.org/10.1016/j.mvr.2012.03.007 (Ex. M). In this study examining blood flow variables after Crestor® treatment, CRP was an independent determinant of the reported increased basal NO activity:

> To address which determinants impact on the improved vascular function due to rosuvastatin treatment, we performed further analyses of our data (Table 2). These analyses revealed **that both LDL-cholesterol and CRP-levels are independent determinants of basal NO activity improvement, expressed as change of cAIx@75 due to L-NMMA infusion, after rosuvastatin treatment**. Furthermore, improved basal

> NO activity is an independent determinant of PP [pulse pressure] amplification as well as pulse wave reflection.

Id. at 3 (emphasis added).

32. Schneider's results showed that statin treatment resulted in both lipid dependent and independent increases in basal NO activity:

> Analysing the determinant factors, we could show that both, namely non- and lipid-dependent effects of statin treatment were related to the improvement of basal NO activity. This is in line with the established view, that the beneficial effect of statins are not solely explained by reducing the synthesis of cholesterol and hence by lowering cholesterol concentrations in the blood. Moreover, by blocking the HMG-CoA reductase also the mevalonate pathway and the production of isoprenoids are inhibited. This accounts for the so-called pleiotropic effects of statin treatment, which includes, among others, enhancing the stability of atherosclerotic plaques, decreasing oxidative stress, vascular inflammation and improving or restoring of endothelial function.

Id. at 4.

The non-lipid factors include CRP. As noted above, CRP level was an independent determinant of basal NO activity improvement. In other words, the decrease in CRP from pre- to post-treatment for the Crestor® group (1.88±2.2 mg/dL vs. 1.17±0.7 mg/dL) resulted in improved basal NO bioavailability in hypercholesterolemic subjects. *See Id*. at 3 and Table 1 baseline characteristics of the study cohort.

33. In sum, Schneider's group has shown that Crestor® improves basal NO bioavailability in hypercholesterolemic patients and that CRP is an independent determining factor in this improvement.

34. AstraZeneca's own scientists have published on the effect of statin administration on NO production and plaque stabilization stating:

> The proposed mechanisms underlying the clinical benefits of therapy with statin drugs, which inhibit 3-hydroxy-3-methylglutaryl coenzyme-A (HMG-CoA) reductase, include depletion of plaque lipid, decreased inflammation, and increased nitric oxide (NO) production. NO has antithrombotic and vasodilator effects and produces many effects similar to other antioxidants. A thicker fibrous cap is formed and there is overall plaque stabilization. The proinflammatory cytokines also stimulate the liver with increased release of C-reactive protein (CRP) and serum amyloid A into the systemic circulation (Figure 2). Statin therapy is associated with reductions in CRP levels.

Donald B. Hunninghake, *Cardiovascular Disease in Chronic Obstructive Pulmonary Disease*, 2 Proc. Am. Thorac. Soc. 44-49, 44-45 (2005) (Ex. N).

35. Dr. Ridker and colleagues have shown the following tying CRP to hypertension, a topic I discuss in more detail below:

> C-reactive protein was significantly associated with and increased risk of developing hypertension in all prespecified subgroups evaluated, including those with very low level of baseline BP, as well as those with no traditional coronary risk factors. Similar results were found when treating C-reactive protein as a continuous variable and controlling for baseline BP.

Howard D. Sesso et al., *C-Reactive Protein and the Risk for Developing Hypertension*, 290 JAMA 2945-2951, 2945 (2003) (Ex. O).

Hypertension

36. Dr. Ridker and colleagues have explained that"[c]oncordant population studies support a relationship between hypertension and atherosclerotic cardiovascular disease consistently and convincingly." Peter Libby and Paul M. Ridker, *Inflammation and Atherothrombosis: From Population Biology and Bench Research to Clinical Practice*, 48 J. Amer. Coll. Cardiol. A33-A46, A34 (2006) (Ex. P).

37. As noted above, CRP is associated with hypertension and an induction of the prothombic milieu. Armed with this data, others groups looked for a cause and effect relationship. One such study, "test[ed] the hypothesis that chronic CRP elevation induces hypertension in mice." Wanpen Vongpatanasin et al., *C-Reactive Protein Causes Downregulation of Vascular Angiotensin Subtype 2 Receptors and Systolic Hypertension in Mice*, 115 Circulation 1020-1028, 1020 (2007) (Ex. Q).

38. This group confirmed that an increased level of CRP was the cause of the hypertension:

> In the present study we have demonstrated that CRP causes a sustained increase in BP in mice and that it is primarily systolic hypertension. In addition, we have shown that the increase in BP induced by CRP is related to an augmented pressor response to angiotensin II that is associated with a reduction in vascular AT_2 expression. These findings provide the first causal linkage between elevations in CRP, the renin–angiotensin system, and hypertension.

Id. at 1024.

39. Since it is well known that elevated CRP levels indicate decreased NO, other groups examined whether elevated CRP levels leading to hypertension were related to this decrease.

40. Hongjing Guan et al., examined "the effects of sustained CRP expression on blood pressure and potential mechanisms of CRP-induced hypertension using in vivo and ex vivo approaches." *Adeno-Associated Virus-Mediated Human C-Reactive Protein Gene Delivery Causes Endothelial Dysfunction and Hypertension in Rats*, 55 Clinical Chemistry 274-284, 275 (2009) (Ex. R).

41. Guan et al. reported the following findings from their study:

> CRP overexpression was associated with impaired endothelial-dependent relaxation, increased arterial stiffness, and decreased NO production. Furthermore, ex vivo and in vivo studies revealed that CRP increased aortic ET-1, ET_A, and AT_1 expression and decreased AT_2 and eNOS expression, and that the effects of CRP on ET-1, ET_A, AT_1, and AT_2 were likely mediated by decreased NO production.

Id. at 282.

Guan et al also reported:

> In the present study, we observed that CRP gene transfer attenuated eNOS expression at both the mRNA and protein levels, similar to previous findings. In addition, ex vivo experiments demonstrated that eNOS protein expression in aortic tissue was decreased after incubation with CRP. Our data indicate a direct inhibitory effect of CRP on eNOS expression.

Id.

42. I also note that studies have shown that statins improve endothelial function in hypertensive animals via increased NO production:

> The important findings of this study are as follows. First, HMG-CoA reductase inhibitor [statins] improved endothelium-dependent vasodilatation of the aorta in the hypertensive animal model, SHR. Second, the improvement of endothelial function by HMG-CoA reductase inhibitor was accompanied by enhanced plasma nitrite and nitrate level reflecting the enhanced production of nitric oxide in endothelium. Third, HMG-CoA reductase inhibitor enhanced the phosphorylation of the eNOS to increase the level of activated eNOS, and subsequently, enhanced the production of nitric oxide without altering the expression level of eNOS.

> Finally, HMG-CoA reductase inhibitor decreased the expression of caveolin-1 in endothelium of aorta, which could modulate the degree of phosphorylation and, ultimately, enhance the activity of the eNOS.

Jung-Won Suh et al., *HMG-CoA Reductase Inhibitor Improves Endothelial Dysfunction in Spontaneous Hypertensive Rats Via Down-regulation of Caveolin-1 and Activation of Endothelial Nitric Oxide Synthase*, 25 J Korean Med Sci, 16-23, 20 (2010) (Ex. S).

43. The data and results are clear: elevated CRP levels are associated with plaque instability, hypertension, and decreased NO. Statins, such as Crestor®, increase NO production to the benefit of the patient.

The Practice of Medicine—What a Medical Doctor Does

44. I am a medical doctor and have been treating patients for about 40 years. During this time, the technology and science may have changed, but the quality of care for my patients has been constant.

45. Like other physicians, I am required to stay up to date on the current treatments, drugs or any other type of relevant patient care modality. And like other physicians, I keep current in many different ways. I attend Continuing Medical Education classes, better known as CMEs. I read the journals in my field to stay on top of the most current scientific data available. Cardiovascular doctors like myself read journals like those listed above such as Circulation, JAMA, and the New England Journal of Medicine, and receive internet updates from websites such as www.heart.org. We attend conferences to present our findings, to listen to other doctors present their own findings, and to simply talk to our fellow doctors and exchange tips, ideas and thoughts about current and

prospective treatments methods. We discuss what drugs we prescribe and for what conditions.

46. Doctors do all of this because a new drug or therapy or surgical procedure might change the calculus of life-saving care, or more likely, life-enhancing care. It is better to prevent a heart attack through prophylactic care than to rehabilitate a patient after the attack. In sum, I (and doctors in general) take the information described above and distill it into better care for our patients. But we are not alone in analyzing patient care data.

47. The great expanse of information available through to internet to my patients makes them better informed about their own care. A Reader's Digest article describes this phenomenon as it relates to cardiovascular medicine.

48. Reader's Digest reports that "[t]he same chemical responsible for men's erections (and, indirectly, for the success of Viagra) also plays a vital role in the health of your arteries, and thus your heart." *Heart Disease Risk Factor #1: Nitric Oxide The Role of Nitric Oxide in Cardiovascular Health*, Reader's Digest, http://www.rd.com/health/heart-disease-risk-factor-1-nitric-oxide/, last accessed on March 29, 2012. (Ex. T).

49. The Reader's Digest publication provides a description for the general public about the scientific data discussed above, for example similar to scientific journals above, this publication discusses endothelial dysfunction:

> If doctors could measure endothelial function — how blood vessels behave — they would have a good indication of your nitric oxide production, and in fact, your overall risk for coronary heart disease (CHD). Measuring endothelial function is like asking your arteries, "How's it going?" If the answer is "well," your arteries are happy with the composition of the blood and are probably relatively free of plaque.

Id.

50. Further, the Reader's Digest article discusses how endothelial health corresponds to NO production:

> All of the major culprits in heart disease — overweight, lack of exercise, smoking, high cholesterol, high blood pressure, high levels of homocysteine and lipoprotein (a) — damage the endothelium. And a damaged endothelium doesn't make enough NO, which results in more damage in an increasingly dangerous spiral.

Id. Reader's Digest quotes John P. Cooke, M.D., Ph.D., head of Stanford University's vascular unit and one of the first researchers to pinpoint the role of NO in cardiovascular health, as stating "The lining of the vessel is very important for cardiac health." *Id*. Dr. Cooke also likens healthy blood vessels to "Teflon" where things "don't stick" and damaged or unhealthy blood vessels to "Velcro, attracting blood-borne gunk like flies to flypaper." *Id*.

51. Over the course of my career working in the field of cardiovascular care and in the course of my continuing educational activities (described above), I have become aware of certain principles that I believe are well known and accepted by the majority of doctors in my field, including (i) NO plays a critical role in maintaining cardiovascular health and NO deficiency is implicated in all cardiovascular disease, (ii) insufficient NO production and/or bioavailability will lead to a decline in that subject's cardiovascular health, and may lead to cardiovascular conditions such as hypertension and an increased risk cardiovascular events such as stroke, (iii) an elevated CRP level in a subject corresponds to decreased NO production and/or bioavailability, and indicates a subject who is at an increased risk for cardiovascular conditions and events, and (iv) statins including

Crestor® increase NO production and/or bioavailability and thus will provide a medical benefit to patients who have decreased NO production and/or bioavailability, including decreasing the subject's risk of cardiovascular conditions and events.

Patient Care

52. The last topic I will discuss is how "heart" doctors care for their patients. We provide thorough history and evaluations like all other physicians. We run tests and look for abnormalities. We use modern technology to diagnose, and modern drugs and surgical techniques to treat.

53. As discussed above, at Roper St. Francis, we use ultrasound for vascular screening the carotid arteries, screening for abdominal aortic aneurysm and ankle-brachial index measurements with blood pressure cuffs and Doppler. We also perform cardiac calcium scoring which is determined by CT scanning. Roper St. Francis charges $125 for vascular screening and an additional $125 for cardiac calcium scoring. These fees are what it costs Roper St. Francis to perform the test and cardiovascular screenings are a great deal for the patient. In fact, at cost cardiac screenings are great deals for everyone. As a matter of policy for the general good of the population in and around Charleston, Roper St. Francis offers these low rates so that people will get tested, and if needed, treated for potential or actual cardiovascular problems.

54. We provide statins to our patients in need of such treatment. We determine need for statins in a number of ways. One way is through the cardiovascular screening mentioned above, arterial ultrasound and heart calcium determinations. Another approach used by physicians is to test for CRP levels directly as per indications 1.6 and 14.8 of the Crestor® package insert. I note that although physicians are allowed to prescribe drugs for indications that are not specified in the drug's label, and we sometimes do, for example, when we read reliable reports of a new for an approved drug, physicians typically follow the approved indications as listed on the package insert when providing drugs, including statins, to a patient. We also get recommendations from our peers as to what to and how to prescribe statins. In others words, our colleagues often tell us what they think works and why. These opinions come through all of the above mentioned channels such as journal articles, meetings, CMEs and/or informal talks amongst our colleagues.

Dated: April 30, 2012

John W. Hallett, M.D.

John Hallett, M.D.